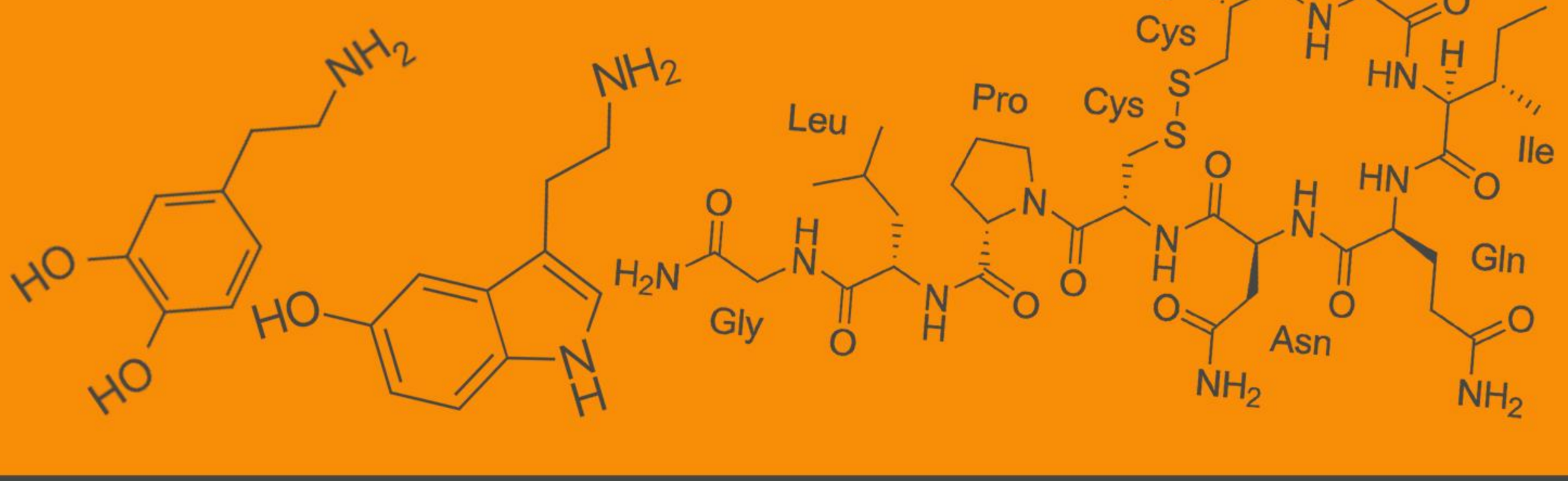
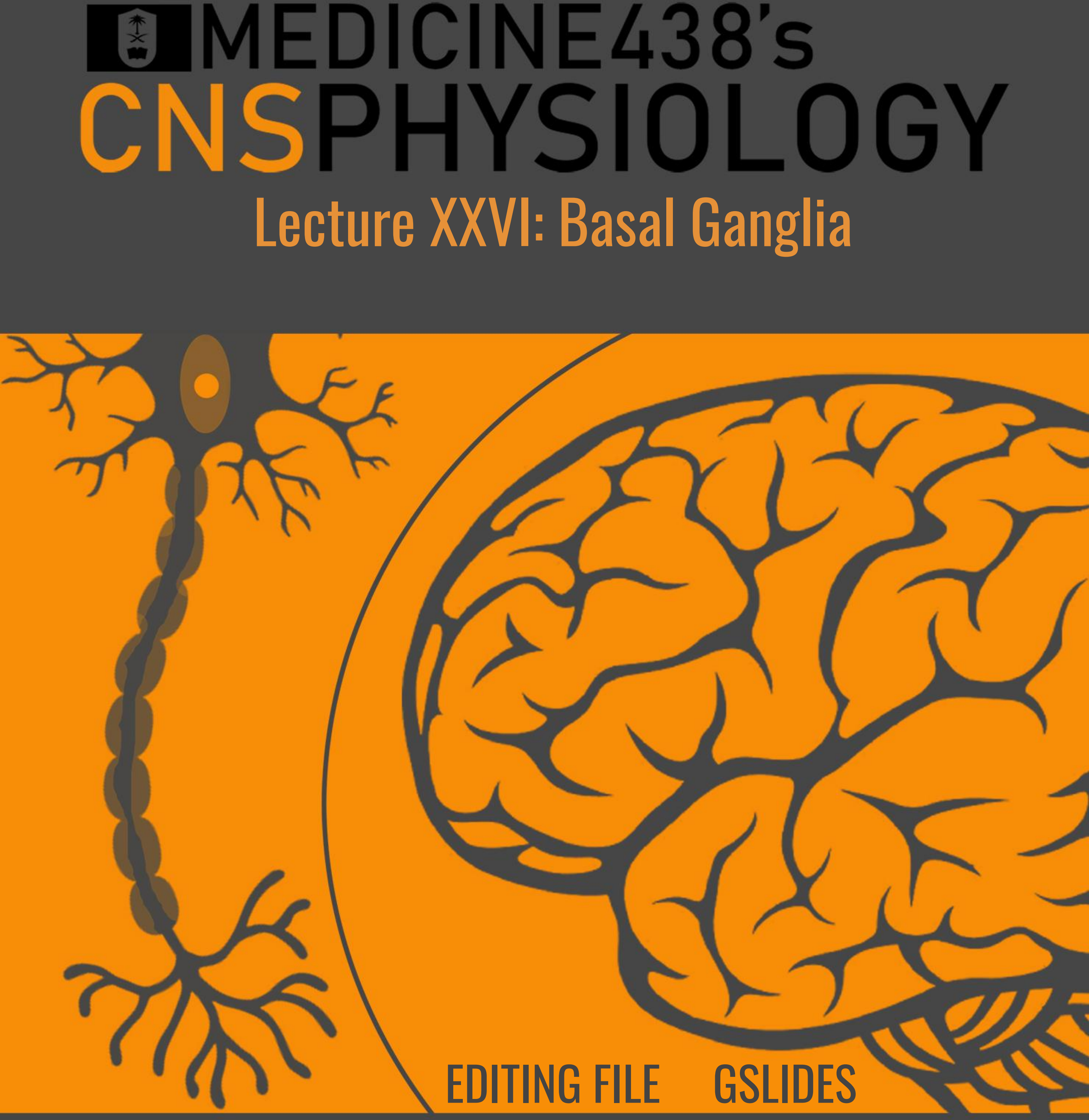


MEDICINE438's CNSPHYSIOLOGY

Lecture XXVI: Basal Ganglia



EDITING FILE GSLIDES

IMPORTANT MALE SLIDES EXTRA FEMALE SLIDES LECTURER'S NOTES

1 BASAL GANGLIA

Lecture Twenty Six

OBJECTIVES

Females objectives :

- **Appreciate different nuclei of basal ganglia .**
- **Know different neurotransmitters that have a role in basal ganglia functions.**
- **Appreciate general functions of basal ganglia.**
- **Diagnose basal ganglia disorders.**

Males Objectives :

- **Describe functional divisions of basal ganglia .**
- **Enumerate basic circuits of movements control.**
- **Explain caudate and putamen circuits.**
- **Explain direct and indirect pathways with neurotransmitters.**
- **appreciate general functions of basal ganglia.**
- **Diagnose basal ganglia disorders.**

BOX 26-1: INTRODUCTION

READY, SET, GO!

With all of what we know about the functions of the motor cortex, cerebellum and prefrontal cortex, it's hard to pinpoint the exact function of the basal ganglia. However, we will give a brief review of motor systems here, and how do they correlate with the basal ganglia.

- Let us try to examine a scenario, suppose a person was stranded in a jungle and was approached by a lion, how would this person begin to run?
- **Readiness:** Signals about body image and position in space are constructed in the **posterior parietal cortex** from visual and proprioceptive inputs. This area makes extensive connections with the prefrontal cortex, an important area for making decisions and planning. The **prefrontal cortex** makes decisions by using sensory input as well as information from the memory, this allows it to make a more informed decision about situations. The prefrontal cortex will notice something is wrong, and will communicate the command to run away from the lion to the association motor areas **premotor area (PMA)**, and **supplementary motor area (SMA), thus making us ready.**
- **Set** PMA and SMA, make motor programs for complex movements, they receive the signal to run, and so they begin to construct the sequence of excitation required and the areas to be stimulated in the primary motor cortex to accomplish the movement, however, these motor programs **sets** up the body for movement, however, for these motor programs to reach the primary motor cortex and initiate movement, it will need the approval of one important structure, the basal ganglia, which will give the **go** signal!
- **Go** The basal ganglia receives signals about intended movements from PMA and SMA, and in turn sends back excitatory signals back to these same areas as well as the primary motor cortex! This positive feedback loop helps provide the motor association areas with the threshold required to initiate movement. Which is basically what the basal ganglia is all about. And the person will begin to run.

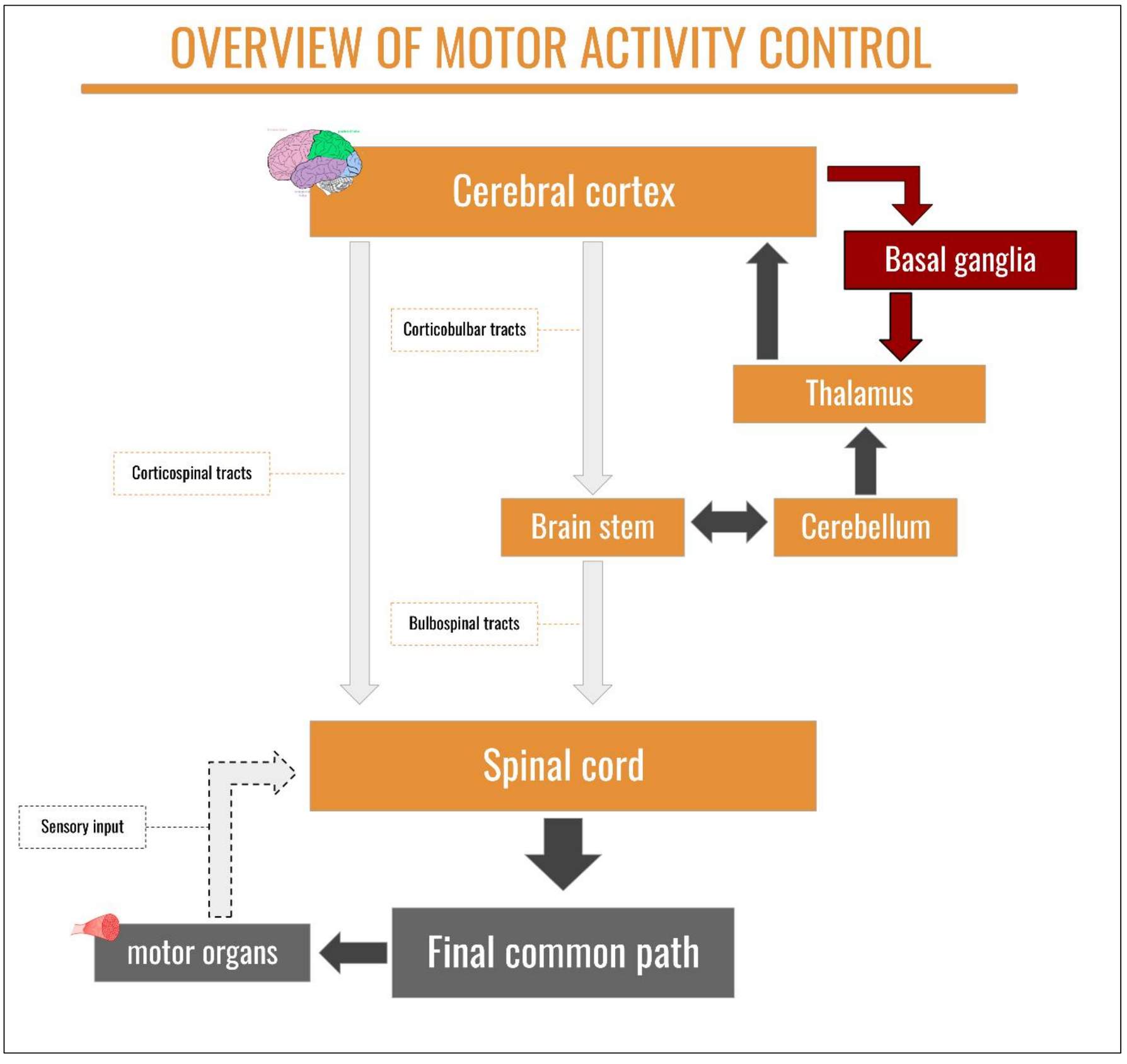


Figure 26-1 Showing the different pathways of motor signals

Basal Ganglia Components And Functional Anatomy

- Caudate nucleus.
- Globus pallidus[2].
- Substantia nigra.[1]
- putamen.
- Subthalamic nucleus.[1]

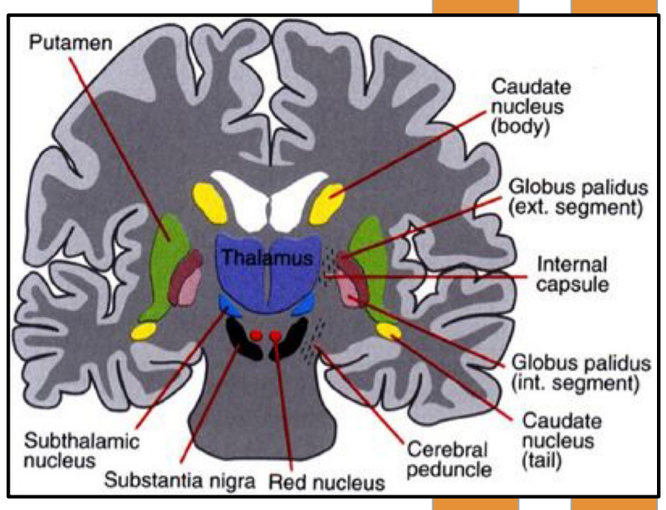


Figure 26-2

- Putamen and Globus pallidus together are called **lentiform nucleus.**

- Caudate nucleus and putamen together are called **Neostriatum (striatum).**

- Caudate nucleus and lentiform nucleus together are called **Corpus striatum.**

Neostriatum		Lenticular Nucleus
Caudate nucleus	Putamen	Globus pallidus
Subthalamic Nucleus		Substantia Nigra

Table 26-1 components of basal ganglia

Functions Of Basal Ganglia

- Control of movements.
- Planning and programming of movements.
- Cognitive control in movements.

Basal Ganglia Connections

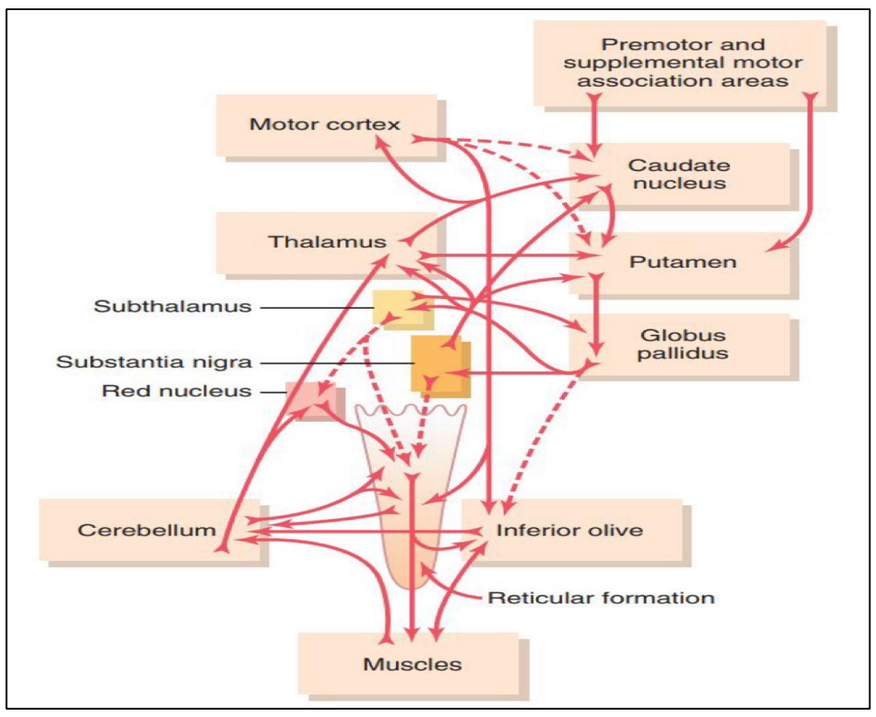


Figure 26-3 Complex Circuitry of Motor Control.

There are three connections to remember

1- Main input to the basal ganglia

2- Main output from the basal ganglia

3-Connections between parts of basal ganglia

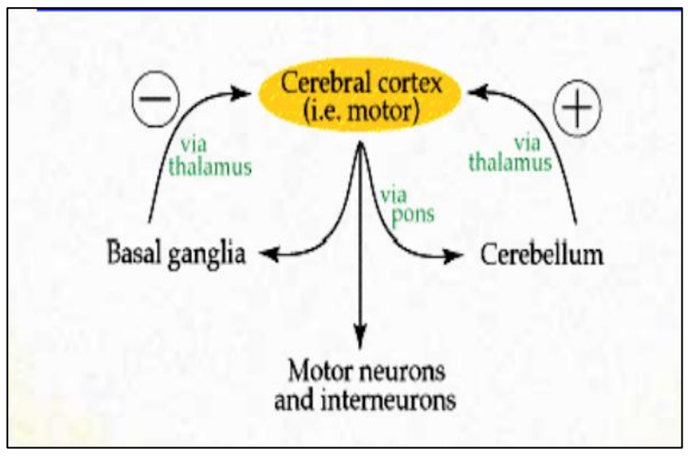


Figure 26- 4 showing the connections of basal ganglia and cerebellum to the cortex ,and their effects in the muscle tone.

FOOTNOTES

1. Dr.shahid: Substantia nigra and subthalamic nucleus are considered functional parts of basal ganglia, but anatomically they are not.
2. It's **important** to point out that globus pallidus externa and interna as well as substantia nigra's pars reticulata are all considered pacemaker cells, that is, they are spontaneously excited, like cardiac nodal cells, and in the case of globus pallidus interna, constantly inhibiting the cortex.

Main Input And Output Of Basal Ganglia

Input	Output
Directly connected to cortex	**Not** Directly connected to cortex
Comes from the cerebral cortex (motor area) and projects to the **NEOSTRIATUM.** (a term for the caudate nucleus and putamen)	Is via the **thalamus** to the cerebral cortex (motor area).

Table 26-2

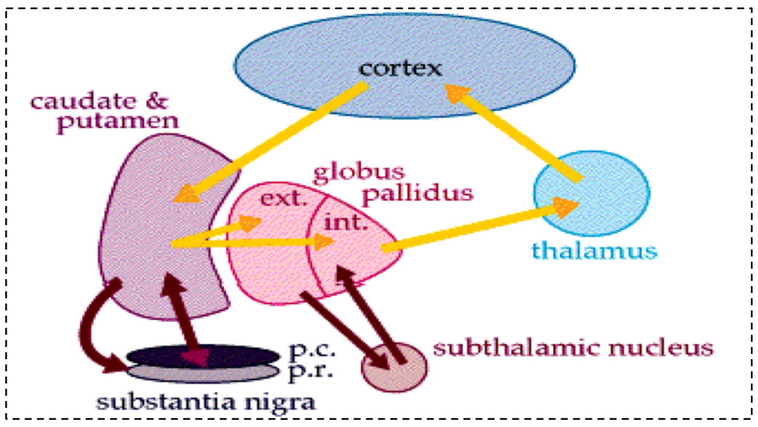


Figure 26-5 Input and output of basal ganglia

BASIC CIRCUITS OF BASAL GANGLIA:

Cognitive loop (Caudate circuit)	• Concerned with cognitive control of sequences of motor pattern. • Basically it is concerned with motor intentions. (Note: **Cognition means the thinking processes of the brain, using both sensory input to the brain plus information already stored in memory.**)
Motor loop (Putamen circuit)	Concerned with learned movement.
Limbic loop	involved in giving motor expression to emotions like, smiling, aggressive or submissive posture. (Via nucleus accumbens reward circuit)[1] Damage to this loop leads to facial masking (also known as hypomimia) which is most commonly associated with Parkinson's disease.
Oculomotor loop	concerned with voluntary eye movement [saccadic movement][2]

Table 26-3

FOOTNOTES

1. Part of the mesolimbic pathway of dopamine, which connects the ventral tegmental area of midbrain to partly, the nucleus accumbens, important for reward, addiction, and emotional behavior. Dysfunction of this pathway leads to schizophrenia and hallucinations.
2. Saccadic eye movements: smooth movements of the eyes from one point of fixation to another point of fixation.

Putamen Circuit

Outputs	Inputs
1. Primary motor cortex 2. Premotor cortex 3. Supplemental motor areas	**2.** Premotor cortex **3.** Supplemental motor areas **4.** Somatosensory Cortex

Table 26-4 A

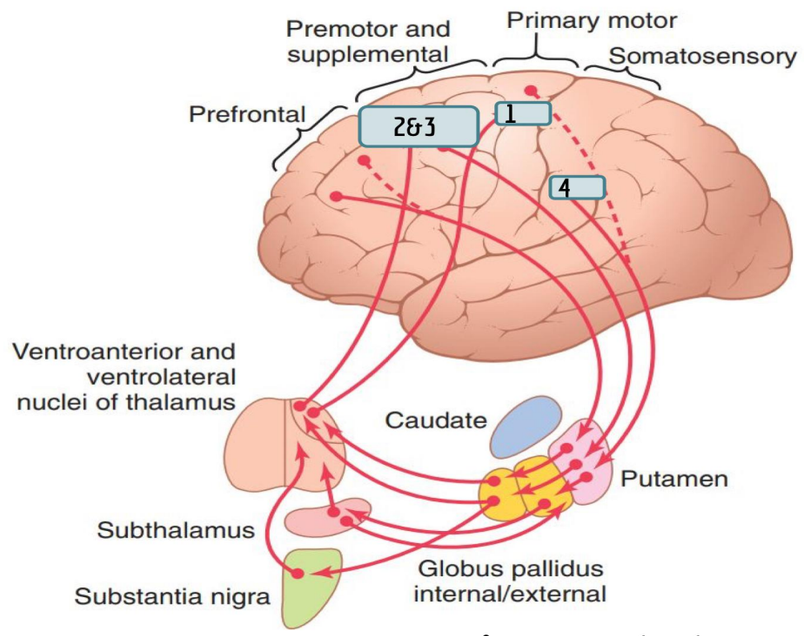


Figure 26-6 A

Functions of the Putamen Circuit

1- Executes Learned Patterns of Motor Activity:

- **Basal ganglia function in association with the corticospinal system to control complex patterns of motor activity (performed subconsciously).**

- **Examples**:
  - writing of letters of the alphabet.
  - cutting paper with scissors.
  - hammering nails.
  - shooting a basketball through a hoop.
  - passing a football.
  - throwing a baseball.
  - the movements of shoveling dirt.
  - most aspects of vocalization
  - controlled movements of the eyes.
  - virtually any other of our skilled movements.

most of them performed subconsciously (Without a plan)

Caudate Circuit

Outputs	Inputs
5. Prefrontal **6**. Premotor cortex **7**. Supplemental motor areas	**8**. Association areas (Association areas provide more understanding of the movement)

Table 26-4 B

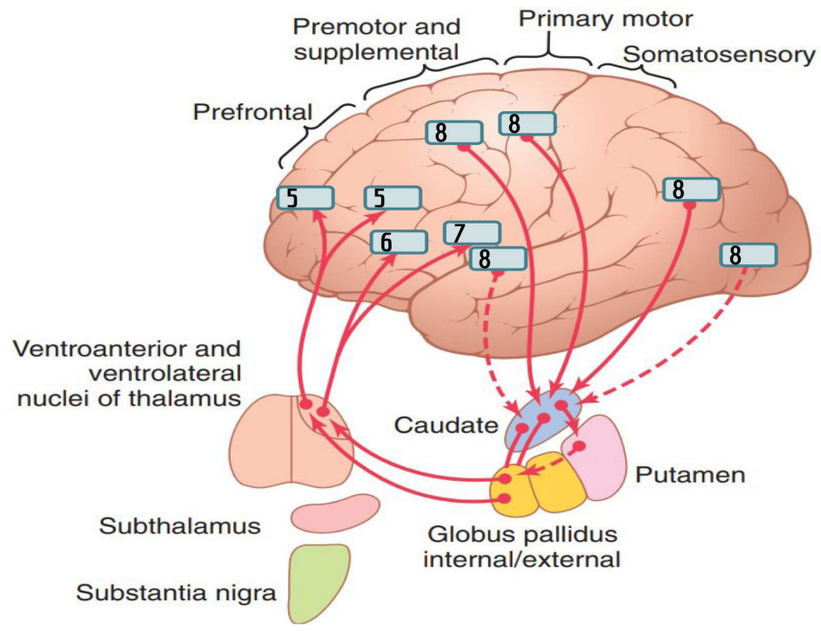


Figure 26-6 B Note that it does not pass through substantia nigra and subthalamus

Functions of the Caudate Circuit

1- Cognitive Control of Sequences of Motor Patterns:

- **Cognition means the thinking processes of the brain, using both sensory input to the brain plus information already stored in memory. Thoughts are generated in the mind by a process called cognitive control of motor activity.**

- **Example:**

A person seeing a lion approach and then responding instantaneously and automatically by:
(1) turning away from the lion,
(2) beginning to run,
(3) and even attempting to climb a tree.
(complete process is explained in BOX 26-1)

Thus, cognitive control of motor activity determines subconsciously, and within seconds which patterns of movement will be used together to achieve a complex goal.

2- Change the Timing and to Scale the Intensity of Movements:

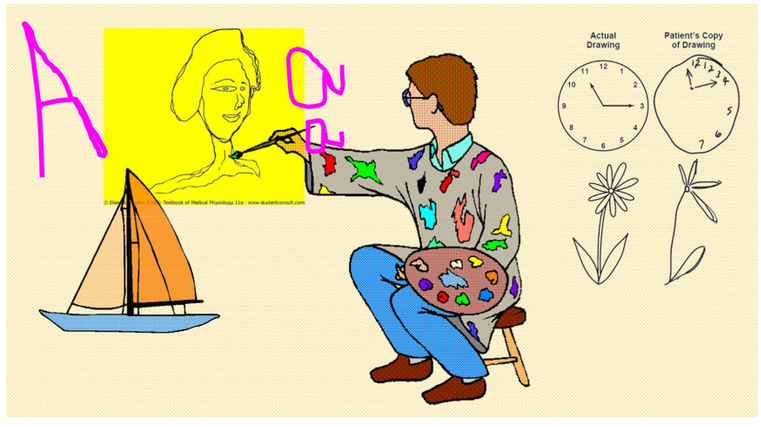
- **Two important capabilities of the brain in controlling movement are:**
  1. **to determine how rapidly the movement is to be performed.**
  2. **to control how large the movement will be.**

- **Example**:

A person may write the letter "a" slowly or rapidly.
Also, he or she may write a small "a" on a piece of paper or a large "a" on a chalkboard.
Regardless of the choice, the proportional characteristics of the letter remain nearly the same.

Damage In Caudate Circuit Results In

- Inability to organize pattern of movements to achieve a complex goal.
- Inability to write or draw figures with fixed scale.
- Loss of timing and scaling of movements.



Basal ganglia pathway (direct vs indirect) :

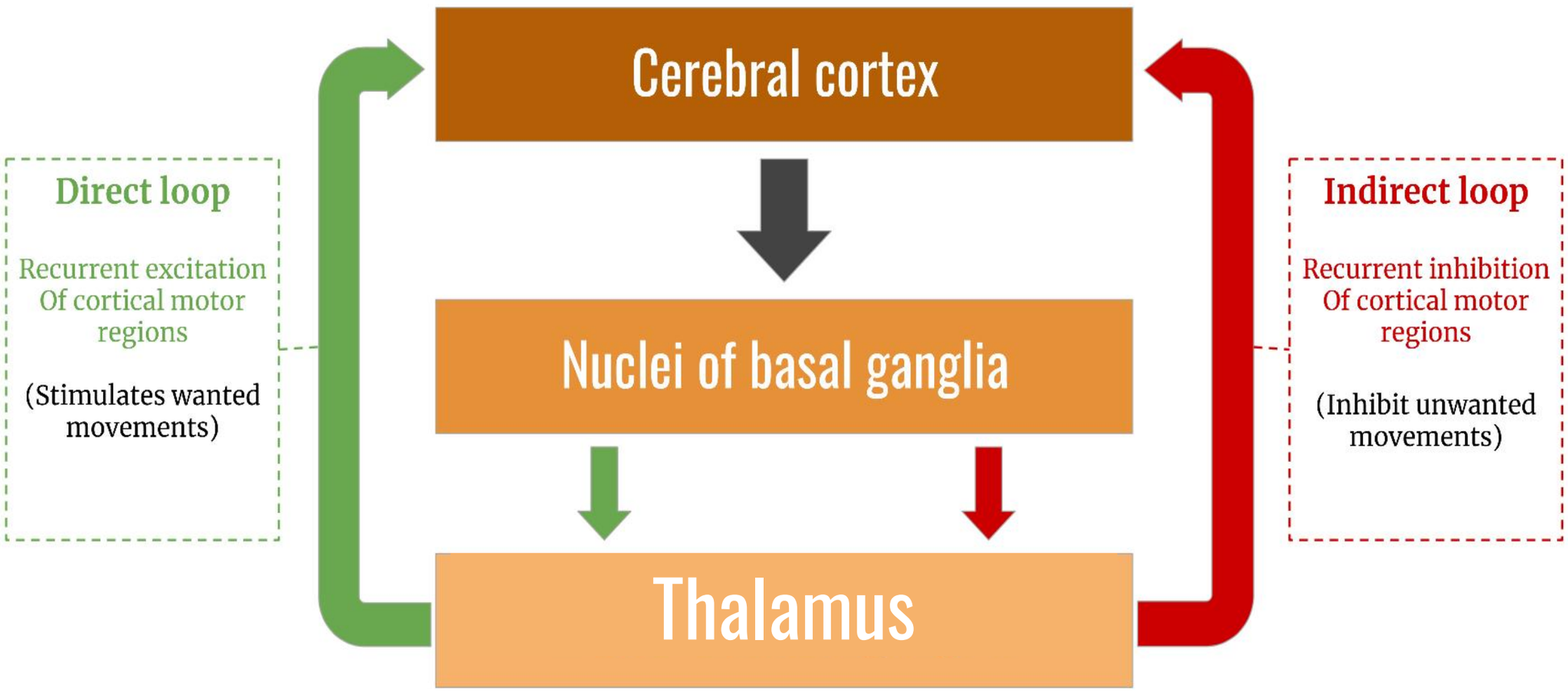


Figure 26- 7 showing how can basal ganglia control motor cortex actions, by either inhibit or stimulate motor cortex regions by 2 different pathways.

Direct and indirect pathways together facilitate action selection, by (female slides):

Direct	Indirect
Activation of direct pathway **facilitates** movement	Activation of indirect pathway **suppresses** movement
Direct output makes focal inhibitory contact on GPi/SNr	Indirect output makes diffuse, widespread excitatory contact on GPi/SNr
Co-activation of these pathways facilitates action selection through center-surround mechanism	

Dopamine effects on direct and indirect pathways (female slides):

Dopamine signaling through **D1** receptors in the direct pathway:

- Facilitates strong, phasic inputs.
- Suppresses weak inputs.

Dopamine signaling through **D2** receptors in the indirect pathway. (suppresses striatal activity)

Basal Ganglia Neurotransmitters & Pathways (Direct and Indirect)[1]

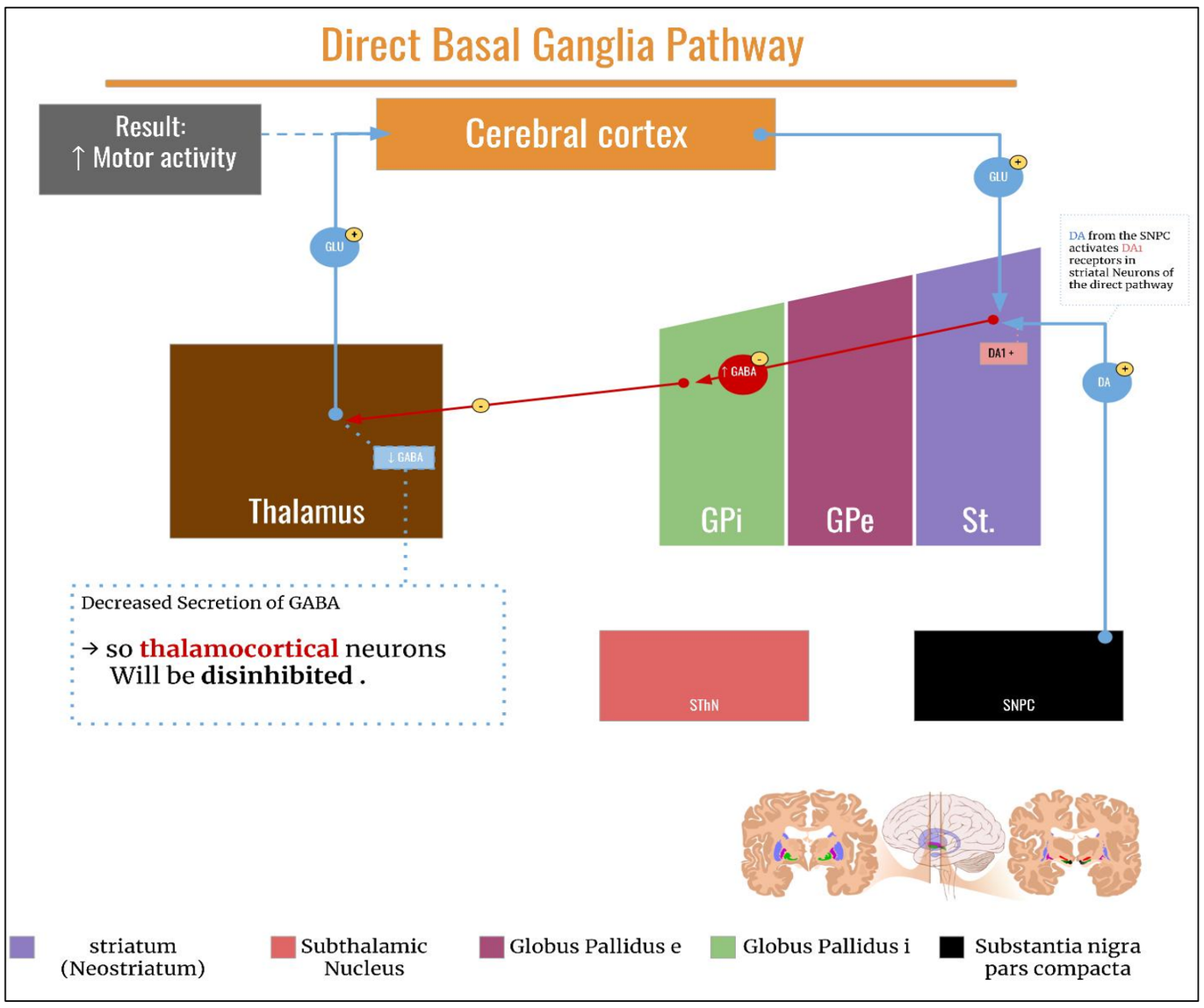


Figure 26-8 A Showing direct basal ganglia pathway. The sequence proceeds as follows: signals from premotor, supplementary and somatosensory cortex excite the striatum (mostly the putamen), the putamen in return sends GABA to inhibit the tonically active pacemaker cell (always firing), the globus pallidus interna, therefore releasing the thalamus from constant inhibition by the basal ganglia and facilitating movement. The striatum also receives significant excitatory signals by SN similar to those from cortex, therefore when SN is degenerated in parkinson's, this pathway will be hypoactive.

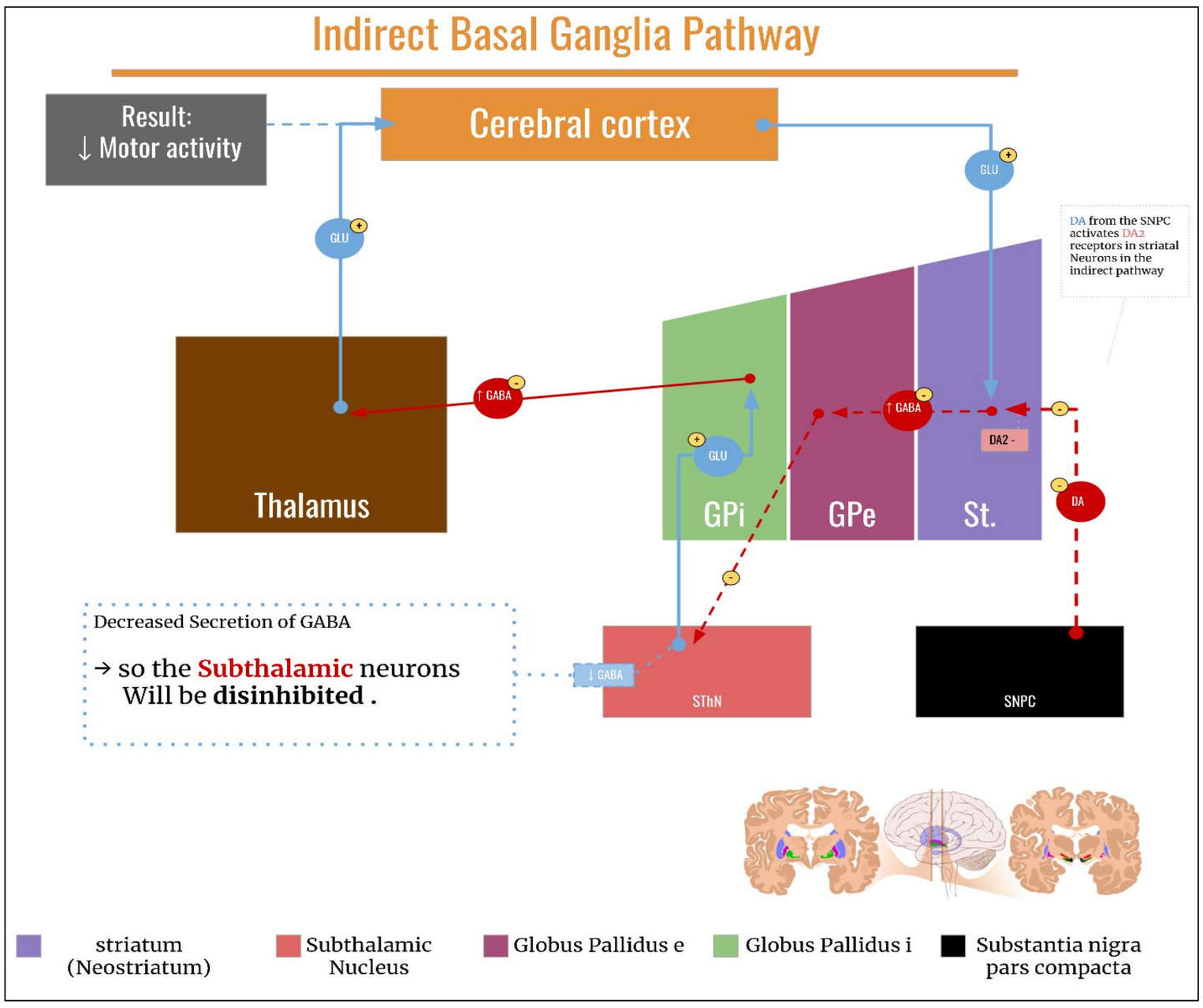


Figure 26-8 B Showing indirect basal ganglia pathway. Striatum receives signals from the cortex's association areas, like the prefrontal cortex, this stimulates the striatum to inhibit the globus pallidus externa (also pacemaker cell) by releasing GABA, globus pallidus externa constantly inhibits subthalamic nuclei, these nuclei have excitatory effects on globus pallidus interna, which remember are constantly working and inhibiting the cortex. Therefore in this pathway when the striatum is excited, it inhibits globus pallidus externa from inhibiting the subthalamus, the subthalamic nuclei become disinhibited, and therefore are excited to stimulate globus pallidus interna, the globus pallidus interna, as we know inhibit the cortex.

FOOTNOTES

1. Dr. Shahid: you should know the neurotransmitter which is released by the fibers in this figure, and the effect of the neurotransmitter.
For example: corticostriatal fibers release glutamate, which is excitatory neurotransmitter.

Disorders Of Basal Ganglia

- Movements Disorders (Ataxia Rate, Range, Force, Direction).
- Speech
- Posture
- Gait
- Mental Activity
- Others

Movements Disorders

Hyperkinetic Lesions affect indirect pathway predominantly	Hypokinetic Lesions affect direct pathway predominantly
• Chorea -Huntington's Disease -Saint Vitus Dance (Sydenham's Chorea)[1] • Athetosis • Dystonia • Hemiballismus/Ballismus • Tardive Dyskinesia • Wilson's Disease.[3]	• Parkinson's Disease • Drug Induced (Neuroleptics, MPTP)[2] • Dopamine receptor blockers eg; Neuroleptics & antipsychotic drugs

Table 26-5

Movement disorder	Lesion	Features
Chorea	Atrophy of the striatum. Ex: Huntington Chorea Saint vitus (post streptococcal infection)	Multiple quick, random movements, usually most prominent in the appendicular muscles
Athetosis	Diffuse hyper myelination of corpus striatum and thalamus	Slow writhing movements,which are usually more severe in the appendicular[4] muscles
Hemiballismus	Hemorrhagic destruction of contralateral subthalamic n. Ex: Hypertensive patients	Wild flinging movements of half of the body
Parkinsonism	Degeneration of Substantia Nigra	Pill rolling tremor of the fingers at rest, lead pipe rigidity and akinesia
Tardive dyskinesia (Boys slides only)	Neuroleptic drugs blocking dopaminergic transmission	Either temporary or permanent uncontrolled involuntary movements of the face and tongue and cogwheel rigidity

Table 26-6 list of movements disorders of basal ganglia.

FOOTNOTES

1. Is a manifestation of rheumatic fever caused by Streptococcal infection, remember rheumatic fever is caused by host's immune response against own tissue due to similarities between host antigens and pathogen antigens, by molecular mimicry, a process we explained early on n our lectures.
2. A prodrug to the neurotoxin MPP+, which causes permanent symptoms of Parkinson's disease by destroying dopaminergic neurons in the substantia nigra of the brain. It has been used to study disease models in various animal studies.
3. Wilson's disease: a rare genetic disorder which causes excessive copper build up, especially in the brain and liver.
4. Referring to the limbs.

Parkinson's Disease

Described by James Parkinson

- Degeneration of dopaminergic nigrostriatal neurons (60-80 %).
- Phenothiazine (tranquilizers drugs).
- Methyl-Phenyl-Tetrahydropyridine (MPTP). The oxidant MPP+ is toxic to SN.

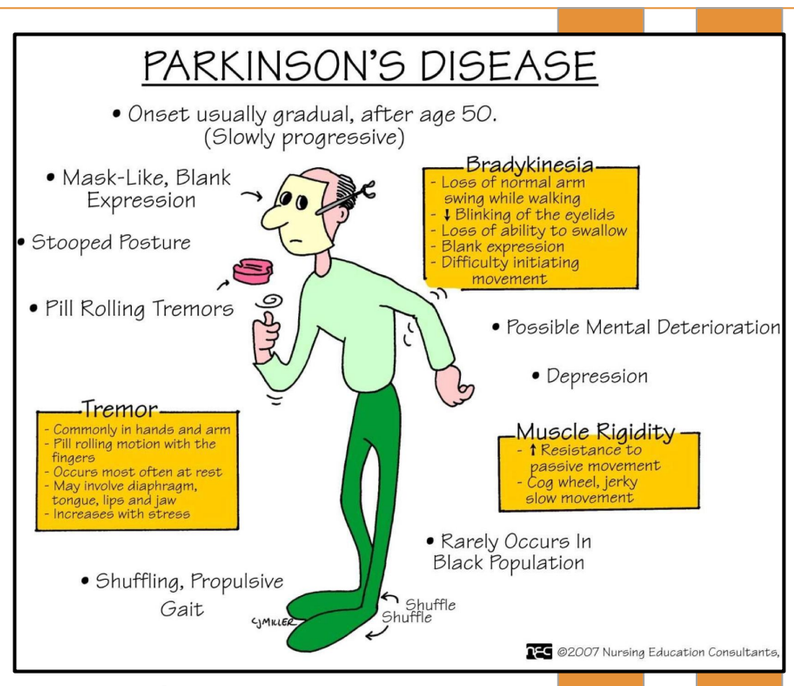


Figure 26-9

5 cardinal features (TRAPS)::

– Tremor
– Rigidity
– Akinesia (difficulty in initiation of movements)
–Bradykinesia (slowness in executions of movements)
– Postural Changes
– Speech Changes

These symptoms are due loss of function of basal ganglia which is involved in coordination of body movements.

(Loss of dopamine = loss of excitatory effect on direct pathway and lose inhibition of indirect pathway)

Treatment:

Levodopa (L-dopa)	Deep brain stimulation (surgery)
• Biosynthetic precursor of dopamine. • Increase dopamine in the brain. • Main treatment used to decrease motor dysfunction. • Absorbed from proximal duodenum. • Protein-restricted diet. • Vit B6 should not be co-administered with dopa. • L-dopa exhibit a large first pass effect. • Only about 1 % reaches brain tissue.	• Brain pacemaker, sends electrical impulses to brain to stimulate the subthalamic nucleus. • Improves motor functions and reduce motor complications. • Complications include: brain hemorrhage, seizures, death.

Table 26-7 showing the surgical and pharmacological treatment of parkinson's diseases

Metabolic Characteristics

- High Oxygen consumption.
- High Copper content in Wilson's disease (Copper intoxication):
  - Autosomal Recessive.
  - Copper binding protein Ceruloplasmin is low.
  - Lenticular degeneration occurs.

QUIZ

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1. Which of the following neural fibers release dopamine in basal ganglia?
A) corticostriatal fibers .
B) striatopallidal fibers.
C) nigrostriatal fibers.
D) Thalamocortical fibers.

2. Lesion to which of the following structures can lead to hemiballismus?
A) striatum .
B) substantia nigra.
C) subthalamic nucleus.
D) globus pallidus.

3. main input to the basal ganglia is through which of the following?
A) thalamus.
B) Neostriatum.
C) globus pallidus.
D) subthalamic nucleus.

4. which of the following basal ganglia circuits is concerned with motor intention and control the sequence of motor patterns.
A) cognitive loop.
B) motor loop.
C) Limbic loop.
D) oculomotor loop.

5. which one of the following disorders is considered a hypokinetic disorder?
A) Wilson's disease.
B) hemiballismus.
C) Athetosis.
D) Parkinson's disease.

6. Which one of the following areas is considered an Input to caudate circuit ?
A) prefrontal cortex.
B) association areas.
C) supplementary area.
D) premotor area.

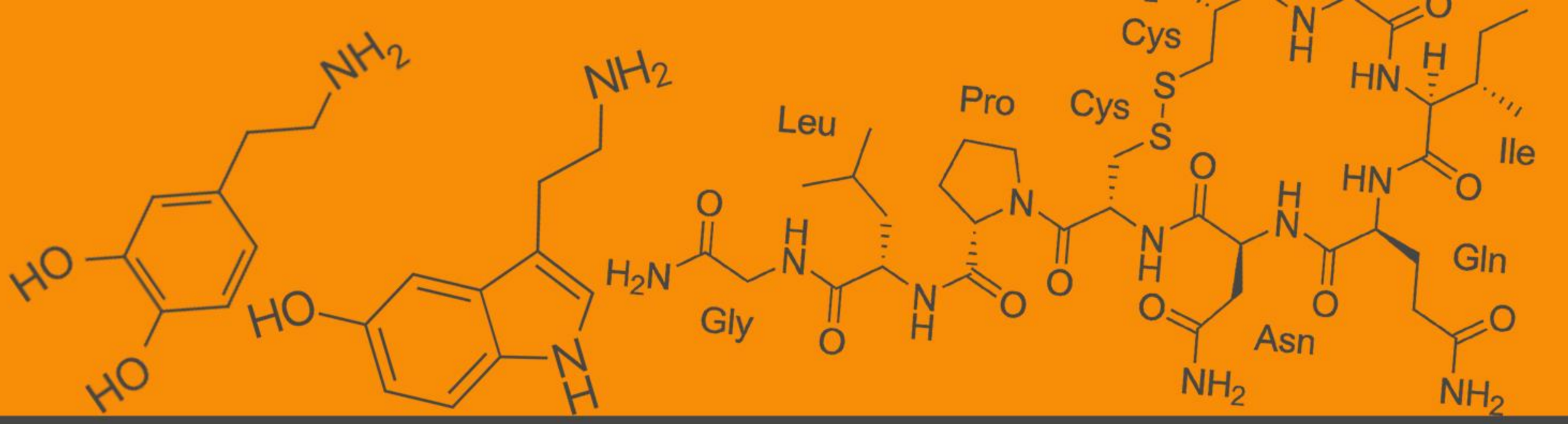
SHORT ANSWER QUESTIONS

1. List one function of the putamen circuit and the caudate circuit.

ANSWERS

1. Putamen: execution of learned movements. Caudate: Timing and scaling the intensity of movements.

ANSWER KEY : C, C, B, A, D, B



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REFERENCES

- Guyton and Hall Textbook of Medical Physiology
- Ganong's Review of Medical Physiology